



## Does a reduced sensitivity to bitter taste increase the risk of becoming nicotine addicted?

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### Abstract

Cigarette smoking appears to be on the increase in adolescents. The initiation of regular smoking nearly always begins before adulthood. It is therefore crucial to find ways of identifying those children most vulnerable to nicotine addiction and prioritizing them for preventive measures. We hypothesized that individuals who, in a simple taste test, perceive phenylthiocarbamide (PTC) as bitter may find the taste of cigarettes aversively bitter and could therefore have a reduced vulnerability to nicotine addiction compared to nontasters, who would be the group at greater risk of addiction. We studied 242 Plains American Indians, 136 women and 106 men aged 18–59 years, and found that (allowing for gender differences and the possible direct effects of smoking on taste) the proportion of PTC nontasters to tasters in smokers, even light smokers, was significantly greater than in both nonsmokers and social smokers ( $\chi^2 = 15.875$ , 4 *df*,  $P = .003$ ), suggesting that nontasters, who are not aversive to the bitter taste of cigarettes, may be more at risk for heavy smoking and therefore more vulnerable to nicotine addiction. © 2001 Elsevier Science Ltd. All rights reserved.

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### 1. Introduction

Cigarette smoking is a major health hazard, yet it is potentially preventable. Approximately one quarter of the adult population smokes; current smoking is positively associated with younger age, lower income, and reduced educational achievement (Bergen & Caporaso, 1999). Regular smoking is nearly always initiated before adulthood. It is particularly disturbing that

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smoking among adolescents is on the rise and is being experimented with at increasingly younger ages (US Surgeon General, 1991). Starting smoking early in adolescence is associated with heavier smoking (Taioli & Wynder, 1991) and a lower likelihood of quitting (Khuder, Dayal, & Mutgi, 1999). In order to improve the chances of preventing the onset of regular smoking in adolescents, it would be beneficial to be able to identify those young children who are at greater risk of addiction and target them for intensified preventive measures. In this study we sought to identify through a simple, cheap taste test, the phenylthiocarbamide (PTC) test, a group of individuals who might be at greater risk for becoming addicted to nicotine.

Individuals vary in their perception of bitterness: less than 60% of Asian Indians, 70% of Caucasians, 90% of Southeast Asians, and 97% of West Africans perceive PTC, a thiourea, as bitter, whereas remaining individuals find it tasteless (Guo, Shen, Wang, & Zheng, 1998; Tepper, 1998). There is a bimodal distribution for PTC taste threshold: low thresholds are classified as tasters, high thresholds as nontasters. PTC taste sensitivity is autosomally dominant and is best described by a two-locus model in which one locus controls PTC tasting and the other controls a more general taste sensitivity (Olson, Boehnke, Neiswanger, Roche, & Siervogel, 1989). Taster status is somewhat higher in women than in men (Bartoshuk, Duffy, & Miller, 1994; Yamauchi, Endo, & Yoshimura, 1995). Taste sensitivity declines with age (Drewnowski, 1990; Parveen, Goni, & Shah, 1990; Yamauchi et al., 1995). PTC tasters often have an aversion for bitter-tasting foodstuffs: beer, caffeine, saccharin, and thiourea-containing cruciferous vegetables, such as broccoli, brussel sprouts, spinach, cabbage, and turnips (Bartoshuk et al., 1994). Nicotine is generally perceived as bitter (Scott, Giza, & Yan, 1998).

Alcoholism and smoking are often comorbid: more than 80% of alcoholics smoke cigarettes (National Institute on Alcohol Abuse and Alcoholism [NIAAA], 1998). As with smoking, serious drinking often starts in adolescence; indeed approximately 40% of alcoholics develop their first symptoms between 15 and 19 years (Helzer, Burnam, & McEvoy, 1991). Several studies show that beer, bitter-tasting to PTC tasters, is the favored drink among adolescents and it has been found that PTC supertasters consume less beer than nontasters when they first start drinking regularly (Intranuovo & Powers, 1998).

We hypothesized that since PTC tasters may find cigarettes aversively bitter, taster status may confer some protection against nicotine addiction in the same way that some Southeast Asian individuals with nonfunctioning variants of alcohol metabolizing enzymes (who as a result have a very unpleasant acetaldehyde-related flushing reaction when drinking even small amounts of alcohol) are protected from alcoholism (Enoch & Goldman, 1999). We chose to test this hypothesis in a Plains American Indian tribe because we believed that as there is a high prevalence of alcoholism in this tribe, there would also be a high prevalence of nicotine addiction. In addition we knew that, perhaps for traditional and cultural reasons, there is widespread exposure to, and use of, tobacco in this tribe. PTC taster status among American Indians is largely unknown and another aim of the study was to establish the prevalence.

## **2. Methods**

We recruited 347 adult tribal members (197 women, 150 men) who essentially formed one large pedigree. Subjects were ascertained for an alcoholism study in which alcoholic

probands were recruited from a treatment clinic in order of presentation and their family members were then ascertained. Informed consent was obtained according to a human research protocol approved by the Human Research Committee of the NIAAA and the Tribal Council. Diagnoses of alcoholism (alcohol dependence) were assigned according to DSM-III-R criteria (American Psychiatric Association, 1987).

Subjects were questioned about their lifetime smoking histories, including the quantity of cigarettes consumed and the time to the first smoke after waking in the morning. Smoking histories were available for 333 subjects. Smokers were defined as those inhaling  $\geq 10$  cigarettes/day. Light smokers were defined as those smoking 10 cigarettes/day and were, as a group, differentiable by features of nicotine addiction, such as shorter times to first smoke, from subjects who smoked fewer cigarettes and less regularly. These “social smokers” were defined as smoking  $\leq 8$  cigarettes/day to allow for a buffer zone with light smokers. Only six subjects fell into this buffer zone and were excluded. Moderate smoking was defined as  $> 10$  to  $\leq 20$  cigarettes/day; heavy smoking was defined as  $> 20$  cigarettes/day. Only current smokers were included in the analysis. Ex-smokers ( $n = 31$ ), including those now smoking  $< 8$  cigarettes/day, were analysed separately because they may be a distinct subtype different from current smokers (e.g., in PTC status), judging by their ability to give up smoking.

Subjects were asked to describe the taste of commercially available PTC-impregnated test papers (two papers at low PTC concentrations, 7  $\mu\text{g}/\text{paper}$  (Darmo, 1999) when saturated with their saliva. Of the 296 individuals still in the study, 283 unambiguously described the taste as either bitter or without taste. The remaining 13 were excluded from the study.

Because PTC taste sensitivity may diminish with age and because older women were perhaps more likely to be nonsmokers for cultural reasons (female nonsmokers were significantly older than women who smoked at all (ANOVA  $F = 7.123$ ,  $P = .001$ , 2 *df*), we elected to study the association of PTC taste ability with current smoking status in subjects aged 18–59 years. Therefore, 32 women and 9 men  $\geq 60$  years were excluded and we were left with a final data set of 242 individuals (136 women, 106 men).

### 3. Results

In this Plains American Indian tribe, 63% of the total sample of 347 individuals were PTC tasters. The point prevalence of alcoholism was 27% in men and 17% in women. The lifetime and point prevalences of smoking  $\geq 10$  cigarettes/day were high: 56% and 42% in men and 37% and 30% in women, respectively.

Overall, 46% of tribal members were, or had been, smokers ( $\geq 10$  cigarettes/day). The mean number of cigarettes/day was 17.8, S.D. = 8.1. Subjects smoked for a mean of 21 years; the mean time to the first smoke after waking was 30 min. Thirty-one percent were social smokers ( $\leq 8$  cigarettes/day). The mean number of cigarettes/day was 3.5, S.D. = 1.8, the modal value was 3 cigarettes/day. Subjects had smoked “socially” for a mean of 15 years. Twenty-three percent of tribal members were nonsmokers.

From Table 1, which shows PTC taster status in current cigarette smokers and nonsmokers aged 18–59 years, it can be seen that the proportion of PTC nontasters to tasters in both

Table 1

PTC taster status in current cigarette smokers and nonsmokers aged 18–59 years

	<i>n</i>	Tasters	Non-tasters	Percent nontasters
Nonsmokers	56	42	14	25
Social smokers ( $\leq 8$ cigarettes/day, mean = 3.5, S.D. = 1.8)	89	66	23	26
Light smokers (10 cigarettes/day)	36	18	18	50
Moderate smokers ( $>10 \leq 20$ cigarettes/day, mean = 19.2, S.D. = 1.9)	51	25	26	51
Heavy smokers ( $>20$ cigarettes/day, mean = 35.0, S.D. = 6.5)	10	5	5	50
Total	242	156	86	36

$\chi^2$  test for tasters vs. nontasters = 15.875, 4 *df*,  $P = .003$ .

nonsmokers and social smokers is 1:3. However, in smokers, even those smoking only 10 cigarettes/day, the proportion is 1:1. The differences in PTC taster status between all groups of smokers and nonsmokers is significant ( $\chi^2 = 15.875$ , 4 *df*,  $P = .003$ ).

There was no significant difference in the length of time that social smokers had been smoking (14.8 years, S.D. = 10.5) compared with light smokers (18.5 years, S.D. = 10.6,  $P = .084$ ). Moderate smokers had been smoking for the same length of time as light smokers (19.9 years, S.D. = 12.1,  $P = .55$ ). However, those smoking heavily,  $>20$  cigarettes/day, had been smoking for much longer (28.6 years, S.D. = 10.1,  $P = .008$  vs. moderate smokers), yet the nontaster/taster proportion was the same as in other categories of smokers, suggesting that smoking history did not have an impact on bitterness detection.

One possibility for changes in bitterness perception might be the impact of alcohol abuse. However, in the 190 tribal members who were not currently drinking, i.e., either nonalcoholics or recovering alcoholics, there was the same significant difference in PTC nontaster/taster ratio between the groups: 1:3 in nonsmokers and social smokers and 1:1 in smokers ( $\chi^2 = 15.1$ ,  $P = .005$ , 4 *df*), implying that alcohol ingestion did not play a role in alteration of bitterness detection.

Although more women were tasters (71%) than men (56%) ( $P = .012$ ), as found in other studies (Bartoshuk et al., 1994), yet the same differences in PTC taster status between smokers and nonsmokers were observed in both sexes and was significant in the larger group of women ( $\chi^2 = 11.3$ , 4 *df*,  $P = .023$ ).

Finally, there was a nonsignificant trend for a difference in the PTC nontaster/taster ratio between ex-smokers ( $n = 24$ ) compared with current smokers ( $n = 97$ ) (1:2 vs. 1:1,  $P = .13$ , age  $< 60$  years). Ex-smokers were significantly older than current smokers (45.0 years S.D. = 10 vs. 38.6 years S.D. = 9.5,  $P = .005$ ) and had smoked more heavily (22.0 vs. 17.4 cigarettes/day,  $P = .009$ ).

#### 4. Discussion

In this Plains American Indian tribe who form essentially one large pedigree, 63% of the total sample of 347 individuals were PTC tasters, a similar prevalence to that found in

Caucasians. There is widespread use of tobacco in this community, both in tribal rituals and at social events such as bingo or drinking alcohol. Three quarters of all the adults smoke cigarettes. Half of this group, “social” smokers, have managed to maintain an average of only 3.5 cigarettes/day for 15 years without increasing. These individuals have a significantly higher proportion of PTC tasters, i.e., bitterness tasters, than the other half of smokers who have smoked on average 18 cigarettes/day for 21 years.

One interpretation of these results is that the bitter taste of cigarettes may deter some PTC tasters from smoking more than a few a day and therefore may protect against nicotine addiction. Alternatively, heavy smoking ( $>25$ /day) has been shown to reduce bitterness taste sensitivity (Peterson, Lonergan, Hardinge, & Linda, 1968). However, we found that PTC nontaster/taster ratios were significantly different in those smoking only 10 cigarettes/day (1:1) compared with 3.5/day (1:3) in social smokers, and this change is unlikely to be due to the direct effect of smoking on taste sensitivity. Additionally, as can be seen from Table 1, there was no gradation of nontaster/taster ratios between light (defined as 10/day), moderate (mean = 19.2/day) and heavy (mean = 35/day) smokers as one might expect if the result was due to the direct effect of cigarette smoking on taste perception.

The group of ex-smokers had a nontaster/taster ratio that was halfway (but not significantly) between non/social smokers and current smokers. One interpretation could be that cigarettes were less palatable to PTC-tasting smokers and hence easier to give up. However, it is possible that as the ex-smokers smoked more heavily than the current smokers their bitterness perception may have been modified at the time they were smoking.

The length of time that individuals smoked did not appear to impact on bitterness perception; there was a progressive increase in years of smoking between light (18.5) and heavy (28.6) smokers yet the nontaster/taster ratio (1:1) remained unchanged. In addition, although this sample was initially ascertained for an alcohol study, our results indicate that current alcohol consumption did not affect PTC taste sensitivity.

In conclusion, we have found that nonsmokers and social smokers are significantly more likely ( $P=.003$ ) to have a stronger perception of bitterness than established smokers, even those smoking only 10 cigarettes/day, and this PTC taster trait may afford a degree of protection against becoming addicted to nicotine. Conversely, nontasters, uninhibited by unpleasant taste sensations, may be more susceptible to heavy cigarette consumption and therefore have an increased risk of addiction.

This finding should be replicated in other populations and tested in prospective studies to determine whether PTC nontaster status does in fact predict smoking initiation and nicotine addiction. If this result proves to be valid then this study has demonstrated a simple, cheap method of identifying PTC nontasters at a young age, who may have increased vulnerability to nicotine addiction. However, this would only be one of several vulnerability factors as our results (from Table 1) show that although 57% of nontasters are smokers, yet 31% of tasters are also smokers. As tasters are twice as common in this American Indian tribe (and in Caucasians) as nontasters, to target only nontasters for preventive measures would be to ignore the majority of smokers. Hence, this simple PTC screening test could eventually be used as part of a battery of tests to identify vulnerability factors in young children in order to try to prevent smoking initiation.

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